

Remarks

Applicants submit a new Information Disclosure Statement as requested by the Examiner. The Examiner advises that the references cited on Applicant's Form PTO-1449 filed June 2008 have not been considered due to the fact that copies of the cited references DC and DD where not legible. A copy of the references is being provided along with the required fee.

Claims 1 and 9 are pending. The present set of claims define a method for the treatment of atherosclerosis in a patient in need of such treatment which comprises administering an effective amount of zoledronic acid or a pharmaceutically acceptable salt or hydrate thereof. The claims further define zoledronic acid being administered locally.

The Examiner has rejected claim 1 under 35 U.S.C. 103(a) as being unpatentable over Ross in view of Jordan et al.. The Examiner has rejected claim 9 under 35 U.S.C. 103(a) as being unpatentable over Ross and Jordan as applied to claim 1 and further in view of Duggan. The Examiner argues that one of ordinary skill in the art would have been motivated to utilize zoledronic acid to treat atherosclerosis due to its ability to cause apoptosis of macrophages and would have had a reasonable expectation of success due to the teachings of the prior art. Applicants respectfully disagree.

One of ordinary skill in the art having the references before him would not be motivated to make the proposed modifications to arrive at the claimed invention, *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). Ross describes the mechanisms of disease for atherosclerosis and the nature of the inflammatory response. Ross does not teach or suggest the use of pharmaceutical products to treat atherosclerosis and there is no discussion on the molecular class of compounds that could be useful for treating atherosclerosis. Jordan describes methods of treating antibody-induced anemia. The description of the bisphosphonates in col. 7, lines 23-37 cover all the bisphosphonates currently on the market at the time of filing of the Jordan patent. No specific bisphosphonate is identified as a preferred product. The use of the bisphosphonates, as described in Jordan, are to treat antibody-induced anemia. A person of ordinary skill in the art would not be motivated to use zoledronic acid to treat atherosclerosis as described in the present invention. The Examples in the specification describe the beneficial effects of zoledronic acid when administered. More specifically, Example 5 on page 25 of the specification describes the effects of bisphosphonates, including zoledronic acid, on arterial calcification, valve calcification and plaque stabilization. Zoledronic acid resulted in the conversion of the so-called "vulnerable" or rupture-prone plaques with large, often calcified, lipid-rich cores and thin fibrous caps with inflammatory cell infiltration observed both at baseline and in vehicle treated animals at 22 weeks to a more stable phenotype. In addition, treatment of zoledronic acid resulted in significantly less calcification of the aortic valves compares with placebo-treated animals. Examples 7 and 8 describe the local administration of zoledronic acid as helpful in treating restenosis.

According to the Examiner, Duggan teaches the use of non-limiting bisphosphonate compounds useful for the treatment of atherosclerosis *inter alia* that can be delivered locally in the form of a liposome delivery system. The Examiner argues that it would have been obvious to one of ordinary skill in the art at the time of the invention that "although Duggan does not each specifically mention the use of the bisphosphonate zoledronic acid, the phrase 'non-limiting' examples of Duggan would have included all known bisphosphonates...". Duggan does not correct the deficiencies of Ross and Jordan. Duggan does not provide the motivation for one of ordinary skill in the art to make the proposed modification and arrive at the claimed invention. Therefore, the claimed invention is non-obvious over the cited references because the references do not teach or suggest or provide the requisite motivation for a person of ordinary skill in the art to make the claimed invention. Applicants respectfully request the obviousness rejection be withdrawn from consideration.

Entry of this Response is respectfully requested.

Respectfully submitted,



Oona A. Manzari
Attorney for Applicant
Reg. No. 48,152

Novartis Pharmaceuticals Corp.
Patents Pharma
One Health Plaza, Building 101
East Hanover, NJ 07936-1080
(862) 778-7852

Date: 3/18/09